PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A Longitudinal Survey of Condom Use Across a U.S. Navy and Marine Corps Shipboard Deployment
AUTHORS	Harbertson, Judith; Devera, Kimberly; Scott, Paul; Li, Yuanzhang; Shaffer, Richard; Michael, Nelson; Hale, Braden

VERSION 1 - REVIEW

REVIEWER	King Holmes, MD, PhD University of Washington, Department of Global Health, Seattle, WA, United States
REVIEW RETURNED	19-Dec-2018

GENERAL COMMENTS	This is a very useful time to document the effectiveness of condom use for preventing acquisition of sexually transmitted infections. Past eras for increasing condom promotion have emerged for various reasons. These “condom eras” include times of war, when displacement of men into war zones and separation of families led to emergence of commercial sex; the large increase in transmission of STIs in recent decades among men who have sex with men; and the emergence of HIV infection, which led to increased condom use. Then came the introduction of PrEP, which has been very successful in preventing acquisition of HIV infection, but is now contributing to a rapid return of the epidemic spread of gonorrhea, syphilis, chlamydia, and herpes. There is also evidence that condom use reduces the risk of acquisition of human papilloma virus infection. Further, there is also evidence that other potentially fatal infections may be sexually transmitted (e.g. meningococcal infection, and hepatitis C); and now it is clear that a very large number of other pathogens not previously regarded as sexually transmitted are in fact commonly present in semen, and are likely sexually transmissible. (Salam, Horby, “The Breadth of Viruses in Human Semen” Emerg, Inf Diseases, CDC, Nov, 2017). Studies of the presence of STI pathogens in vaginal fluid has been conducted, and more is planned. Such studies may further motivate a decrease in unprotected sex. Thus, the timing is just right for the report of the excellent study by Judith Harbertson, et al., who have revisited and confirmed the effectiveness of a condom promotion program in the US military for preventing various STIs, and it will likely be true that condom promotion and condom use will eventually be shown to reduce the acquisition and transmission of many other important STIs. Other methods, in addition to promotion of condom use, are needed to contain the spread of HIV and other STIs. These include needle exchange programs to prevent infection by contaminated needles (along with substitution of safer opioids to

	replace more dangerous opioids). In addition, “motivational interviewing” is becoming common in modern clinical medicine to reduce risky behaviors (including risky sexual behaviors); and to promote healthy behaviors. There is evidence for the effectiveness of population-level interventions to prevent STI transmission in LMICs. (Note: I have reviewed the article and written a brief commentary, which describes how this article fits into the key work being done on the prevention and control of STDs Globally, which you are free to use.)

REVIEWER	Minilik Demissie Ethiopian public health Institute (Ethiopia) Lund University (Sweden)
REVIEW RETURNED	14-Jan-2019

GENERAL COMMENTS	Dear Author A longitudinal study is an observational research method in which data is gathered for the same subjects repeatedly over a period of time. Nevertheless, as you mention in the manuscript methods part line 120 to 122 most of the participants from t1 to t3 are different individuals. thus this is not a longitudinal study since it doesn't fulfill the requirement of observation or change over time. as to me, this is three separate crossectional studies which can not be compared. so change the methods and analysis and in the result part do not compare the data as if it is a longitudinal data collected from similar individuals observed through different situations.

REVIEWER	Karine Blouin Scientist, Institut national de santé publique du Québec Associate professor, Université de Montréal Canada
REVIEW RETURNED	02-Feb-2019

GENERAL COMMENTS	This interesting manuscript provides results on condom use during military deployments. As mentioned by the authors, these results may contribute to STI prevention and public health intervention in this specific context and also in wider context. The authors defined transactional sex as sex with a sex worker or giving or receiving sex for money, goods or improved work conditions. Was it possible to separate the act of giving or receiving sex (i.e. dintinguish sex worker or client)? It could have been interesting, especially for deployments in countries with a known high HIV/STI prevalence in sex workers. Why the authors did not report prevalence ratios rather than odds ratios in the multivariate analysis? To my knowledge, the AIC criterion should not be used for model selection with GEE. Why did the authors choose this method to handle missing data (missing indicator)? Even in the scenario where data are considered missing completely at random (MCAR) and there are very few missing

	observations, this method often introduces bias. If this is used for missing data on potential confounder variables, the estimates will be biased due to residual confounding (Pedersen AB, Mikkelsen EM, Cronin-Fenton D, Kristensen NR, Pham TM, Pedersen L, Petersen I. Missing data and multiple imputation in clinical epidemiological research. Clin Epidemiol. 2017 Mar 15;9:157-166. doi: 10.2147/CLEP.S129785. eCollection 2017. PubMed PMID: 28352203; PubMed Central PMCID: PMC5358992). The authors should mention this limit. It would be interesting for the authors to further develop on how these results can be used for public health interventions.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: King Holmes, MD, PhD

Institution and Country: University of Washington, Department of Global Health, Seattle, WA, United States

This is a very useful time to document the effectiveness of condom use for preventing acquisition of sexually transmitted infections. Past eras for increasing condom promotion have emerged for various reasons. These “condom eras” include times of war, when displacement of men into war zones and separation of families led to emergence of commercial sex; the large increase in transmission of STIs in recent decades among men who have sex with men; and the emergence of HIV infection, which led to increased condom use. Then came the introduction of PrEP, which has been very successful in preventing acquisition of HIV infection, but is now contributing to a rapid return of the epidemic spread of gonorrhea, syphilis, chlamydia, and herpes. There is also evidence that condom use reduces the risk of acquisition of human papilloma virus infection. Further, there is also evidence that other potentially fatal infections may be sexually transmitted (e.g. meningococcal infection, and hepatitis C); and now it is clear that a very large number of other pathogens not previously regarded as sexually transmitted are in fact commonly present in semen, and are likely sexually transmissible. (Salam, Horby, “The Breadth of Viruses in Human Semen” Emerg, Inf Diseases, CDC, Nov, 2017). Studies of the presence of STI pathogens in vaginal fluid has been conducted, and more is planned. Such studies may further motivate a decrease in unprotected sex. Thus, the timing is just right for the report of the excellent study by Judith Harbertson, et al., who have revisited and confirmed the effectiveness of a condom promotion program in the US military for preventing various STIs, and it will likely be true that condom promotion and condom use will eventually be shown to reduce the acquisition and transmission of many other important STIs.

Other methods, in addition to promotion of condom use, are needed to contain the spread of HIV and other STIs. These include needle exchange programs to prevent infection by contaminated needles (along with substitution of safer opioids to replace more dangerous opioids). In addition, “motivational interviewing” is becoming common in modern clinical medicine to reduce risky behaviors (including

risky sexual behaviors); and to promote healthy behaviors. There is evidence for the effectiveness of population-level interventions to prevent STI transmission in LMICs.

(Note: I have reviewed the article and written a brief commentary, which describes how this article fits into the key work being done on the prevention and control of STDs Globally, which you are free to use.)

Response: Thank you very much for your comments.

Reviewer: 2 (see attached)

Reviewer Name: Minilik Demissie

Institution and Country: Ethiopian public health Institute (Ethiopia) Lund University (Sweden)

Dear Author A longitudinal study is an observational research method in which data is gathered for the same subjects repeatedly over a period of time. Nevertheless, as you mention in the manuscript methods part line 120 to 122 most of the participants from t1 to t3 are different individuals. thus this is not a longitudinal study since it doesn't fulfill the requirement of observation or change over time. as to me, this is three separate crossectional studies which can not be compared. so change the methods and analysis and in the result part do not compare the data as if it is a longitudinal data collected from similar individuals observed through different situations.

Response: Thank you for your comments. In a longitudinal study, each experimental or observational unit is measured across time. Incomplete data are not unusual under such designs, as many subjects are not available to be measured at all time points. Standard longitudinal data software, such SAS, allowing for unbalanced data, can be used.

In general, there is no essential difference on the regression coefficients of covariates between using longitudinal analysis and using cross sectional analysis, however treating the measurements within subject as independent records without using the GEE approach (eg., cross section analysis) will underestimate the standard error of the covariate, hence overestimate the significance. In addition, it may overestimate the standard error for the time varying covariate.

References:

Missing data methods in longitudinal studies: a review

Joseph G. Ibrahim and Geert Molenberghs

Using GEE in Stata : https://www.ucl.ac.uk/iehc/research/primary-care-and-population-health/research/thin-database/publications/research_presentations/gee

Reviewer: 3

Reviewer Name: Karine Blouin

Institution and Country: Scientist, Institut national de santé publique du Québec Associate professor, Université de Montréal Canada

This interesting manuscript provides results on condom use during military deployments. As mentioned by the authors, these results may contribute to STI prevention and public health intervention in this specific context and also in wider context.

The authors defined transactional sex as sex with a sex worker or giving or receiving sex for money, goods or improved work conditions. Was it possible to separate the act of giving or receiving sex (i.e. dintinguish sex worker or client)? It could have been interesting, especially for deployments in countries with a known high HIV/STI prevalence in sex workers.

Response: Thank you for your suggestion and we agree it would have been more informative to separate out giving vs. receiving money for sex. Unfortunately the question used to collect this information "…did you give or receive sex for any of the following?" combined these two factors so we were unable to examine them separately. This was in part intentional as transactional sex is a Uniform Code of Military Justice (UCMJ) violation and investigators were concerned that service members would be reluctant to report they paid for sex if we had requested that information in a stand-alone question. We did ask in the deployment survey only what type of sexual partner they had sex with, and sex worker was an option. Those analyses are underway and will be reported in a subsequent publication.

Why the authors did not report prevalence ratios rather than odds ratios in the multivariate analysis?

Response: The odds ratio is the default estimated statistic in logistic model. The odds ratio is a suitable estimation for measure the relative risk (prevalence ratio). This statistic attempts to quantify the strength of the association between STI and Condom use. The prevalence estimation of STI is only for the study population (the sample), which might be different than that for general population.

To my knowledge, the AIC criterion should not be used for model selection with GEE.

Response: For GEE, QIC should be reported rather than AIC. If "too many" covariates are used, we may see QIC=0, which means, there are too few subjects with longitudinal data, to evaluate QIC. In such a case, SAS will perform the model without GEE, and report AIC.

QIC or AIC, is used for model selection to judge if too many covariates are added in the model. In fact, this study doesn't use AIC or QIC to select covariates, which may not need to be reported. All covariates including the levels of categorical factors were selected by investigators rather than by AIC or QIC.

Why did the authors choose this method to handle missing data (missing indicator)?

Response: To handle the missing data, we identified the covariates of interest, created a category for "missing" and analyzed the data including the missing category/ data. Doing this has almost no effect when estimating the effect of other levels for that variable and the study population (data used in model) is the same for adding or removing any predictors, for univariate or multiple variate modeling. It allows the effect of control factors to be consistent. Otherwise different models will use different data, because different variables have different missing records.

Even in the scenario where data are considered missing completely at random (MCAR) and there are very few missing observations, this method often introduces bias. If this is used for missing data on potential confounder variables, the estimates will be biased due to residual confounding (Pedersen AB, Mikkelsen EM, Cronin-Fenton D, Kristensen NR, Pham TM, Pedersen L, Petersen I. Missing data and multiple imputation in clinical epidemiological research. Clin Epidemiol. 2017 Mar 15;9:157-166. doi: 10.2147/CLEP.S129785. eCollection 2017. PubMed PMID: 28352203; PubMed Central PMCID: PMC5358992). The authors should mention this limit.

Response: Thank you for the suggestion. No interpolation was used, hence no need to consider MCAR or Missing at Random and EM approach.

It would be interesting for the authors to further develop on how these results can be used for public health interventions.

Response: Thank you for your suggestion. Please see revised text (line 358).

VERSION 2 – REVIEW

REVIEWER	Minilik Demissie Ethiopian public health institute/Lund University, Sweden
REVIEW RETURNED	15-Mar-2019

GENERAL COMMENTS	The reviewer well addressed my concern during revision

REVIEWER	Karine Blouin Institut national de santé publique du Québec et Université de Montréal, Canada
REVIEW RETURNED	15-Mar-2019

GENERAL COMMENTS	Comments were addressed. Very interesting article.